tion Cell Proliferation Assay) was used to determine the number of viable cells at To and the number of cells remaining after 48 hours compound exposure. The number of cells remaining after 48 hours was compared to the number of viable cells at the time of drug addition, allowing for calculation of growth inhibition.

[0956] The growth over 48 hours of cells in control wells that had been treated with vehicle only (0.25% DMSO) is considered 100% growth and the growth of cells in wells with compounds is compared to this. Mitotic kinesin inhibitors inhibited cell proliferation in human ovarian tumor cell lines (SKOV-3).

[0957] A Gi_{50} was calculated by plotting the concentration of compound in μM vs the percentage of cell growth of cell growth in treated wells. The Gi_{50} calculated for the compounds is the estimated concentration at which growth is inhibited by 50% compared to control, i.e., the concentration at which:

$$100\times[(Treated_{48}-T_0)/(Control_{48}-T_0)]=50.$$

[0958] All concentrations of compounds are tested in duplicate and controls are averaged over 12 wells. A very similar 96-well plate layout and Gi_{50} calculation scheme is used by the National Cancer Institute (see Monks, et al., J. NatI. Cancer Inst. 83:757-766 (1991)). However, the method by which the National Cancer Institute quantitates cell number does not use MTS, but instead employs alternative methods.

Example 102

Calculation of IC_{50}:

[0959] Measurement of a composition's IC_{50} uses an ATPase assay. The following solutions are used: Solution 1 consists of 3 mM phosphoenolpyruvate potassium salt (Sigma P-7127), 2 mM ATP (Sigma A-3377), 1 mM IDTT (Sigma D-9779), 5 μM paclitaxel (Sigma T-7402), 10 ppm antifoam 289 (Sigma A-8436), 25 mM Pipes/KOH pH 6.8 (Sigma P6757), 2 mM MgCl2 (VWR JT400301), and 1 mM EGTA (Sigma E3889). Solution 2 consists of 1 mM NADH (Sigma N8129), 0.2 mg/ml BSA (Sigma A7906), pyruvate kinase 7 U/ml, L-lactate dehydrogenase 10 U/ml (Sigma P0294), 100 nM motor domain of a mitotic kinesin, 50 μg/ml microtubules, 1 mM DTT (Sigma D9779), 5 μM paclitaxel (Sigma T-7402), 10 ppm antifoam 289 (Sigma A-8436), 25 mM Pipes/KOH pH 6.8 (Sigma P6757), 2 mM MgC12 (VWR JT4003-01), and 1 mM EGTA (Sigma E3889). Serial dilutions (8-12 two-fold dilutions) of the composition are made in a 96-well microtiter plate (Corning Costar 3695) using Solution 1. Following serial dilution each well has 50 μl of Solution 1. The reaction is started by adding 50 μl of solution 2 to each well. This may be done with a multichannel pipettor either manually or with automated liquid handling devices. The microtiter plate is then transferred to a microplate absorbance reader and multiple absorbance readings at 340 nm are taken for each well in a kinetic mode. The observed rate of change, which is proportional to the ATPase rate, is then plotted as a function of the compound concentration. For a standard IC_{50} determination the data acquired is fit by the following four parameter equation using a nonlinear fitting program (e.g., Grafit 4):

$$y=\frac{\text{Range}}{1+\left(\frac{x}{IC_{50}}\right)^{s}}+\text{Background}$$

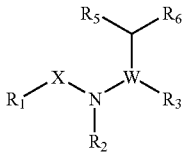
where y is the observed rate and x the compound concentration.

[0960] Other chemical entities of this class were found to inhibit cell proliferation, although GI_{50} values varied. GI_{50} values for the chemical entities tested ranged from 200 nM to greater than the highest concentration tested. By this we mean that although most of the chemical entities that inhibited mitotic kinesin activity biochemically did inhibit cell proliferation, for some, at the highest concentration tested (generally about 20 μM), cell growth was inhibited less than 50%. Many of the chemical entities have GI_{50} values less than 10 μM, and several have GI_{50} values less than 1 μM. Anti-proliferative compounds that have been successfully applied in the clinic to treatment of cancer (cancer chemotherapeutics) have G_{50}'s that vary greatly. For example, in A549 cells, paclitaxel GI_{50} is 4 nM, doxorubicin is 63 nM, 5-fluorouracil is 1 μM, and hydroxyurea is 500 μM (data provided by National Cancer Institute, Developmental Therapeutic Program, http://dtp.nci.nih.gov/). Therefore, compounds that inhibit cellular proliferation at virtually any concentration may be useful.

What is claimed is:

1. At least one chemical entity chosen from compounds of Formula I

Formula 1



and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

R_1 is optionally substituted aryl, optionally substituted heterocyclyl, or optionally substituted heteroaryl;

X is —CO or —SO_2—;

R_2 is hydrogen or optionally substituted lower alkyl;

W is —CR_4—, —CH_2CR_4—, or N;

R_3 is —CO—R_7, hydrogen, optionally substituted alkyl, optionally substituted heterocyclyl, cyano, optionally substituted sulfonyl, or optionally substituted aryl;

R_4 is hydrogen or optionally substituted alkyl;

R_5 is hydrogen, hydroxyl, optionally substituted amino, optionally substituted heterocyclyl; or optionally substituted lower alkyl;

R_6 is hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aryloxy, optionally substituted heteraryloxy, optionally substituted alkoxycarbonyl-, optionally substituted ami-